Remarks

Claims 40-45 and 47-55 are pending in the instant application. Claims 40-44 and 47-55 stand rejected under 35 U.S.C. § 112, first paragraph. Claim 45 stands rejected as directed to an non-elected invention. An appendix of pending claims is attached for the Examiner's convenience.

Election/Restriction

Claim 45 is hereby canceled as directed to a non-elected invention. Applicant reserves the right to pursue the non-elected subject matter in one or more a related applications.

35 U.S.C. §112, First Paragraph

Claims 40-44 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make or use the invention. Specifically, the Examiner argues that a skilled practitioner would have to turn to trial and error experimentation to practice gene therapy with the claimed compositions. Applicants respectfully disagree. Rather than turning to trial and error experimentation to use the claimed compositions to practice gene therapy, the skilled practitioner need only turn, as discussed below, to the specification.

The Examiner asserts that the specification does not provide guidance for one skilled in the art to practice gene therapy. The Examiner is respectively directed to page 17, lines 14-17, which states, "In a preferred embodiment, the gene therapy techniques include the incorporation of the exogenous gene using enhanced homologous recombination (HER), for example as described in PCT/US93/03868, hereby incorporated in its entirety." A copy of PCT/US93/03868 is enclosed for the Examiner's review. Passages providing detailed guidance in the field of gene therapy can be found at Page 33, Line 12 to Page 39, Line 14 as well as a working example where homologously targeted complementary DNA oligonucleotides were used to correct a naturally occurring 3 base pair deletion mutant in a human CF transmembrane conductance regulator (CFTR) allele and restore expression of a functional CFTR protein in targeted

mammalian cells, Page 51, Line 41 to Page 64, Line 11. In light of the extensive guidance provided by the Applicant, withdrawal of this rejection is respectfully requested.

The Examiner further asserts that the Orkin *et al.* reference (Orkin, S.H. & Motulsky, A.G., Report and Recommendations of the Panel to asses the NIH Investment in Research on Gene Therapy, Dec. 7, 1995; WWW.NIH.GOV/news/panelrep.htm(1995)) establishes that gene therapy has not been successfully practiced and that no vector recited in the reference is competent for use in gene therapy. The Examiner goes on to conclude that anyone skilled in the art would have employ trial and error experimentation to practice gene therapy. Applicants respectfully submit that this is a mischaracterization of the Orkin *et al.* reference. First, Orkin *et al.* is not a scientific study, but rather, as the title suggests, a recommendation regarding the future role of the National Institutes of Health in gene therapy research. Accordingly, the statements included in Orkin *et al.* represent the opinions of the authors, rather than scientific fact. Second, far from establishing that gene therapy has not been practiced, Orkin *et al.* explicitly refers to over 100 government approved gene therapy protocols. While the panel preparing this report may have reservations about the design of one or more of these clinical trials, data illustrating the failure of any one of these clinical trials is not presented. Accordingly, it is improper to infer that each and every one of these trials has shown gene therapy to be ineffective. Finally, Table 1 of Orkin et al. does not establish that the listed vectors are unsuitable for gene therapy, as argued by the examiner. Rather, the table lists known advantages and disadvantages of those vectors. It is improper to infer from that table that no known vector is suitable for gene therapy, as the table merely illustrates the fact that one vector may have disadvantages relative to another. In light of the foregoing discussion Applicant respectfully requests withdrawal of the rejection to Claims 40-44.

Claims 47-55 stand rejected under 35 U.S.C. § 112, first paragraph as lacking sufficient written description to reasonably convey to one skilled in the relevant art that the Applicants had possession of the claimed invention at the time of filing. In particular, the Examiner asserts that the specification does not describe human cells with the two recited constructs with such clarity that one of skill in the art would appreciate that the applicants had possession of the cells of Claims 47-55 at the time of the filing of the instant application.

At Page 17, Lines 1-26 the instant application discusses the claimed composition; a human cell comprising a recombinant nucleic acid encoding Rad51 and a recombinant nucleic acid encoding a tumor suppressor protein. This portion of the specification relates to the role of Rad51 in cancer and apoptosis and provides methods for inducing apoptosis in cells. For example, "In a preferred embodiment, the methods comprise increasing the activity of Rad51 in cells...in a preferred embodiment the activity of Rad51 is increased by increasing the amount of Rad51 in the cell, for example by overexpressing the endogenous Rad51, or by administering a gene encoding Rad51, using known gene therapy techniques..." Page 17, Lines 2-14. On that same page the specification includes a tumor suppressor as part of the method to induce apoptosis in the cell: "in a preferred embodiment, the methods further comprise increasing the activity of p53 in the cell, for example by increasing the amount of p53, as outlined above for Rad51." Page 17, Lines 24-26. Additionally, the specification points out, at Page 10, Lines 13 – 18, that human cells are a useful in the practice of this invention. Accordingly, one skilled in the art would appreciate that the applicant possessed the claimed invention at the time of the filing of the application and withdrawal of the rejection to Claims 47-55 is respectfully requested.

Conclusion

Applicants respectfully submit that the claims are now in condition for allowance and an early notification of such is solicited. If, upon review, the Examiner feels there are additional outstanding issues, the Examiner is invited to call the undersigned attorney. This paper is filed under 37 C.F.R. section 1.34(a).

Respectfully submitted,
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Appendix of Pending Claims

40. (Twice Amended) A pharmaceutical composition comprising:

a) nucleic acid encoding a Rad51 protein;

b) nucleic acid encoding a tumor suppressor protein; and

c) a pharmaceutical carrier.

41. (Amended) A composition according to claim 40 wherein said tumor suppressor protein is p53.

42. (Amended) A composition according to claim 40 wherein said tumor suppressor protein is BRCA1.

43. (Amended) A composition according to claim 40 wherein said tumor suppressor protein is BRCA2.

44. (Amended) A composition according to claim 40 comprising:

a) nucleic acid encoding a Rad51 protein;

b) nucleic acid encoding a BRCA1 protein;

c) nucleic acid encoding a BRCA2 protein; and

d) nucleic acid encoding a p53 protein.

47. A human cell comprising a recombinant nucleic acid encoding a RAD51 protein and a recombinant nucleic acid encoding a tumor suppressor protein.

48. A human cell according to claim 47 wherein said tumor suppressor protein is BRCA1.

49. A human cell according to claim 47 wherein said tumor suppressor protein is BRCA2.

50. A human cell according to claim 47 comprising:

a) a recombinant nucleic acid encoding a RAD51 protein;

b) a recombinant nucleic acid encoding a BRCA1 protein;

c) a recombinant nucleic acid encoding a BRCA2 protein; and

d)a recombinant nucleic acid encoding a p53 protein.

51. A human cell according to claim 47 wherein said human cell is a breast tissue cell.

52. A human cell according to claim 47 wherein said human cell is a cancerous breast tissue cell.

53. A human cell according to claim 47 wherein said human cell is a cancerous cell.

54. A human cell according claim 47 wherein said human cell is in a cell culture.

55. A human cell according claim 47 wherein said human cell is isolated.